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(54) Title: IMPROVEMENTS RELATING TO DOUBLE-STRANDED RNA INHIBITION

(57) Abstract: There are described ways of improving the efficiency of double stranded RNA inhibition as a method of inhibiting gene expression in nematode worms such as *C. elegans*. In particular, the invention relates to the finding that changes in the genetic background of *C. elegans* result in increased sensitivity to double-stranded RNA inhibition.

## INTERNATIONAL SEARCH REPORT

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## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/10 C12N9/22 C07K14/435 C12N15/66 C12N15/70  
C12N1/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, WPI Data, PAJ

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	TIMMONS L ET AL: "Specific interference by ingested dsRNA" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 395, no. 6705, 29 October 1998 (1998-10-29), page 854 XP002103601 ISSN: 0028-0836 the whole document	1-4, 12-21, 23-25, 28-31, 34-39
A	FIRE A ET AL: "Potent and specific genetic interference by double-stranded RNA in <i>Caenorhabditis elegans</i> " NATURE, GB, MACMILLAN JOURNALS LTD. LONDON, vol. 391, 19 February 1998 (1998-02-19), pages 806-811, XP002095876 ISSN: 0028-0836 cited in the application the whole document	1-4
-/-		

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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\*A\* document member of the same patent family

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## INTERNATIONAL SEARCH REPORT

International Application No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SHARP PHILLIP A: "RNAi and double-strand RNA." GENES & DEVELOPMENT, vol. 13, no. 2, 15 January 1999 (1999-01-15), pages 139-141, XP002171268 ISSN: 0890-9369 the whole document	1-4
A	RAY C ET AL: "GUT-SPECIFIC AND DEVELOPMENTAL EXPRESSION OF A CAENORHABDITIS ELEGANS CYSTEINE PROTEASE GENE" MOLECULAR AND BIOCHEMICAL PARASITOLOGY,NL,ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, vol. 51, 1992, pages 239-249, XP000572340 ISSN: 0166-6851 abstract	2-4,8
A	RAND J B ET AL: "GENETIC PHARMACOLOGY: INTERACTIONS BETWEEN DRUGS AND GENE PRODUCTS IN CAENORHABDITIS ELEGANS" METHODS IN CELL BIOLOGY,LONDON,GB, vol. 84, 1995, pages 187-204, XP000956211 page 190, paragraph 1 -page 194, paragraph 4	1-4,8
A	AVERY LEON ET AL: "The Caenorhabditis elegans unc-31 gene affects multiple nervous system-controlled functions." GENETICS, vol. 134, no. 2, 1993, pages 455-464, XP001011453 ISSN: 0016-6731 the whole document	2-4,8
A	TAGESSON C ET AL: "INFLUENCE OF SURFACE-ACTIVE FOOD ADDITIVES ON THE INTEGRITY AND PERMEABILITY OF RAT INTESTINAL MUCOSA" FOOD AND CHEMICAL TOXICOLOGY, vol. 22, no. 11, 1984, pages 861-864, XP001009621 ISSN: 0278-6915 the whole document	8

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## INTERNATIONAL SEARCH REPORT

International Application No.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A	<p>LYON CHRISTOPHER J ET AL: "The C. elegans apoptotic nuclease NUC-1 is related in sequence and activity to mammalian DNase II."</p> <p>GENE (AMSTERDAM), vol. 252, no. 1-2, 11 July 2000 (2000-07-11), pages 147-154, XP001009494 ISSN: 0378-1119 abstract; figure 3 page 151, right-hand column, paragraph 2 -page 153, right-hand column, paragraph 2</p>	6,7
P,X	<p>WO 00 01846 A (MORTIER KATHERINE ;DEVGEN NV (BE); BOGAERT THIERRY (BE); PLAETINCK) 13 January 2000 (2000-01-13) cited in the application</p> <p>page 8, line 9 -page 10, line 22 page 12, line 14 -page 23, line 2 figures 5,9; examples 1-4</p>	1-4, 12-21, 23-25, 28-31, 34-39
P,X	<p>WO 00 63425 A (FEICHTINGER RICHARD ;BEGHYN MYRIAM (BE); DEVGEN NV (BE); BOGAERT T) 26 October 2000 (2000-10-26) abstract page 2, line 14-30 page 6, line 18-33 page 7, line 12 -page 9, line 28 page 12, line 20 -page 13, line 25; example 3</p>	2-5,8,9, 29-33
T	<p>TIMMONS LISA ET AL: "Ingestion of bacterially expressed dsRNAs can produce specific and potent genetic interference in Caenorhabditis elegans."</p> <p>GENE (AMSTERDAM), vol. 263, no. 1-2, 2001, pages 103-112, XP001009512 ISSN: 0378-1119 the whole document</p>	1-4, 12-21, 23-26, 28-31, 34-39

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0001846 A	13-01-2000	AU 4907999 A	24-01-2000
		EP 1093526 A	25-04-2001
		GB 2349885 A	15-11-2000
		NO 20010019 A	05-03-2001
WO 0063425 A	26-10-2000	AU 3984600 A	02-11-2000
		GB 2351152 A	20-12-2000

Form PCT/ISA/210 (patent family annex) (July 1992)

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